

IN THE CLAIMS

Please amend the claims as follows:

Claim 1 (Currently Amended): ~~A purified~~ An isolated polynucleotide which encodes a polypeptide ~~that inhibits~~ inhibiting the NF- κ B signaling pathway, said polynucleotide ~~being~~ is selected ~~[[in]]~~ from the group consisting of:

(a) a polynucleotide which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39;

(b) a ~~purified~~ polynucleotide complementary to the ~~one~~ polynucleotide as defined in (a); and

(c) ~~a purified polynucleotide which is at least 70% identical to the polynucleotide as defined in (a);~~

(d) ~~a purified polynucleotide which is at least 80% identical to the polynucleotide as defined in (a);~~

(e) ~~a purified polynucleotide which is at least 90% identical to the polynucleotide as defined in (a) and~~

(f) ~~a purified~~ polynucleotide which hybridizes under stringent conditions to the polynucleotide as defined in (a), wherein said stringent conditions comprise washing in 5X SSC at a temperature from 50 to 68°C.

Claim 2 (Cancelled).

Claim 3 (Currently Amended): The ~~purified~~ isolated polynucleotide of Claim 2, wherein said polypeptide disrupts NEMO oligomerization.

Claim 4 (Currently Amended): A vector comprising the ~~purified~~ isolated polynucleotide of Claim 1.

Claim 5 (Currently Amended): A host cell comprising the ~~purified~~ isolated polynucleotide of Claim 1.

Claim 6 (Currently Amended): ~~A purified~~ An isolated polypeptide ~~that inhibits~~ inhibiting the NF- κ B pathway ~~selected in the group consisting of:~~

a) ~~a NEMO type polypeptide having comprising~~ comprising an amino acid sequence selected ~~from~~ from the group consisting of SEQ ID NO:3, SEQ ID NO:7, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39~~[[;]]~~, wherein said polypeptide is a NEMO type polypeptide.

b) ~~a purified polypeptide which is at least 70% identical to the polypeptide as defined in a);~~

c) ~~a purified polypeptide which is at least 80% identical to the polypeptide as defined in a);~~

(d) ~~a purified polypeptide which is at least 90% identical to the polypeptide as defined in a);~~

(e) ~~a purified polypeptide which is at least 95% identical to the polypeptide as defined in a);~~

Claim 7 (Cancelled).

Claim 8 (Currently Amended): The ~~purified~~ isolated polypeptide of Claim ~~[[7]]~~ 6, wherein said polypeptide disrupts NEMO oligomerization.

Claim 9 (Currently Amended): A polypeptide fusion construct that inhibits the NF- κ B pathway, said construct comprising an amino acid sequence ~~being selected in the group consisting of:~~

~~a) a polypeptide fusion construct comprising an amino acid sequence selected [[in]] from the group consisting of SEQ ID NO: 3, SEQ ID NO:7, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39, wherein said amino acid sequence and which is linked to a polypeptide having a high transduction potential;~~

~~b) a polypeptide fusion construct comprising an amino acid sequence at least 80% identical to an amino acid sequence as defined in a);~~

~~c) a polypeptide fusion construct comprising an amino acid sequence at least 90% identical to an amino acid sequence as defined in a);~~

~~d) a polypeptide fusion construct comprising an amino acid sequence at least 95% identical to an amino acid sequence as defined in a);~~

~~e) a polypeptide fusion construct comprising an amino acid sequence that is at least 70% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 7, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, and SEQ ID NO: 39;~~

~~said amino acid sequence being linked to a polypeptide having a high transduction potential.~~

Claim 10 (Original): The polypeptide of Claim 9, wherein said polypeptide fusion construct disrupts NEMO oligomerization.

Claim 11 (Currently Amended): The polypeptide of Claim 9, ~~wherein said~~ which is linked ~~[[is]]~~ by an amino acid spacer sequence having a length ranging from 1-35 amino acids.

Claim 12 (Original): The polypeptide of Claim 11, wherein said amino acid spacer sequence is selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO: 10.

Claim 13 (Original): The polypeptide of Claim 9, wherein said polypeptide having a high transduction potential has an amino acid sequence of SEQ ID NO: 1.

Claim 14 (Original): The polypeptide of Claim 13, wherein the polypeptide fusion construct has the amino acid sequence selected in the group consisting of SEQ ID NO: 2, SEQ ID NO: 6, SEQ ID NO:13 and SEQ ID NO:15.

Claim 15 (Currently Amended): A method of inhibiting the NF- κ B signaling pathway comprising contacting *in vitro* an eukaryotic cell with a polypeptide fusion construct of ~~Claims 9 to 14~~ Claim 9.

Claim 16 (Currently Amended): A method of disrupting NEMO oligomerization comprising contacting *in vitro* said NEMO with a polypeptide fusion construct of ~~Claims 9 to 14~~ Claim 9.

Claim 17 (Currently Amended): ~~Use of an effective amount of a composition~~ A method of treating a disorder regulated by the NF- κ B signaling pathway comprising administering an effective amount of a composition comprising a polypeptide fusion construct of ~~Claims 9 to 14~~ Claim 1 and one or more pharmaceutically acceptable carriers or excipients, for the preparation of a medicament for modulating or treating a disorder regulated by the NF- κ B signaling pathway in to a subject in need thereof.

Claim 18 (Currently Amended): The ~~[[use]]~~ method of Claim 17, wherein said subject in need thereof is a human.

Claim 19 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 17 or 18~~ Claim 17, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

Claim 20 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 17 to 19~~ Claim 17, wherein said disorder regulated by the NF- κ B signaling pathway is selected from the group consisting of inflammatory responses, oncogenesis, and viral infection.

Claim 21 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 17 to 20~~ Claim 17, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

Claim 22 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 17 to 21~~ Claim 17, wherein said composition is administered preferably intravenously.

Claim 23 (Currently Amended): ~~Use of an effective amount of a~~ A method for regulating cell proliferation or apoptosis comprising administering an effective amount of a composition comprising a polypeptide fusion construct of ~~Claims 9 to 14~~ Claim 9 and one or more pharmaceutically acceptable carriers or excipients, ~~for the preparation of a medicament for regulating cell proliferation or apoptosis in~~ to a subject in need thereof.

Claim 24 (Currently Amended): The ~~[[use]]~~ method of Claim 23, wherein said subject in need thereof is a human.

Claim 25 (Currently Amended): The ~~[[use]]~~ method of Claim 23 ~~or Claim 24~~, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

Claim 26 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 23 to 25~~ Claim 23, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

Claim 27 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 23 to 26~~ Claim 23, wherein said composition is administered preferably intravenously.

Claim 28 (Currently Amended): ~~Use of an effective amount of a~~ A method for regulating B or T lymphocytes in antigenic stimulation comprising administering an effective amount of a composition comprising a polypeptide fusion construct of Claims 9 to 14 Claim 9 and one or more pharmaceutically acceptable carriers or excipients, for the preparation of a medicament for regulating cell proliferation or apoptosis in to a subject in need thereof.

Claim 29 (Currently Amended): The ~~[[use]]~~ method of Claim 28, wherein said subject in need thereof is a human.

Claim 30 (Currently Amended): The ~~[[use]]~~ method of Claim 28 ~~or Claim 29~~, wherein said effective amount ranges from 0.1 mg/Kg/day to 30 mg/Kg/day.

Claim 31 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 28 to 30~~ Claim 28, wherein said composition is administered in a form selected from the group consisting of oral, rectal, nasal, parenteral, intracisternal, intravaginal, intraperitoneal, sublingual, topical, and bucal administration.

Claim 32 (Currently Amended): The ~~[[use]]~~ method of ~~Claims 28 to 31~~ Claim 28, wherein said composition is administered preferably intravenously.

Claim 33 (Original): A method of identifying polypeptides that modulate oligomerization of NEMO comprising:

- a) identifying a candidate polypeptide sequence;
- b) creating a polypeptide fusion construct by linking said candidate polypeptide sequence to a polypeptide having a high transduction potential via a spacer sequence;

- c) contacting a cell culture with the polypeptide fusion construct; and
- d) monitoring the activity of the NF- κ B signaling pathway;
- e) comparing the activity of the NF- κ B signaling pathway in the presence of said polypeptide fusion construct to the activity of the NF- κ B signaling pathway in the absence of said polypeptide fusion construct to determine the relative inhibition by said polypeptide fusion construct; and
- f) correlating relative inhibition by said polypeptide fusion construct to NEMO oligomerization.

Claim 34 (Original): The method of Claim 33, wherein said candidate polypeptide sequence has a coiled-coil or helical structure.

Claim 35 (Currently Amended): The method of Claim 33 ~~or Claim 34~~, wherein said candidate polypeptide sequence has 20-60 amino acids.

Claim 36 (Currently Amended): The method of ~~Claims 33 to 35~~ Claim 33, wherein said candidate polypeptide sequence is derived from NEMO.

Claim 37 (Currently Amended): The method of ~~Claims 33 to 36~~ Claim 33, wherein said spacer sequence has a length ranging from 1-35 amino acids.

Claim 38 (Original): The method of Claim 37, wherein said spacer sequence is selected from the group consisting of SEQ ID NO: 9 and SEQ ID NO: 10.

Claim 39 (Original): The method of Claim 33, wherein said polypeptide having a high transduction potential has an amino acid sequence of SEQ ID NO: 1.

Claim 40 (Currently Amended): The method of Claim 33, wherein said cell culture comprises pre-B 70Z/3 lymphocytes that have been transfected with a NF- κ B dependent β -galactosidase reporter gene, ~~deposited at the CNCM (Collection Nationale de Cultures de Microorganismes), 28 rue du Docteur Roux, 75724 PARIS Cedex 15, France, on April 1st, 2003 under number I 3004.~~

Claim 41 (Original): The method of Claim 33, wherein said polypeptide fusion construct further comprises an N-terminal cysteine residue.

Claim 42 (Original): The method of Claim 39, further comprising:

b-1) labeling said polypeptide fusion construct; and

c-1) monitoring cellular uptake of the labeled polypeptide fusion construct.

Claim 43 (Original): The method of Claim 42, wherein said labeling comprises chemically reacting the cysteine residue with a fluorophore.

Claim 44 (Original): The method of Claim 43, wherein said fluorophore is BODIPY.

Claim 45 (Original): The method of Claim 42, wherein said monitoring cellular uptake is by FACS.

Claim 46 (New): The isolated polynucleotide of Claim 1, which is at least 70% identical to the polynucleotide according to (a).

Claim 47 (New): The isolated polynucleotide of Claim 1, which is at least 80% identical to the polynucleotide according to (a).

Claim 48 (New): The isolated polynucleotide of Claim 1, which is at least 90% identical to the polynucleotide according to (a).

Claim 49 (New): The isolated polynucleotide of Claim 1, which is at least 95% identical to the polynucleotide according to (a).

Claim 50 (New): The isolated polypeptide of Claim 6, which is at least 70% identical to said amino acid sequence.

Claim 51 (New): The isolated polypeptide of Claim 6, which is at least 80% identical to said amino acid sequence.

Claim 52 (New): The isolated polypeptide of Claim 6, which is at least 90% identical to said amino acid sequence.

Claim 53 (New): The isolated polypeptide of Claim 6, which is at least 95% identical to said amino acid sequence.

Claim 54 (New): The fusion construct of Claim 9, wherein said polypeptide is at least 70% identical to said amino acid sequence.

Claim 55 (New): The fusion construct of Claim 9, wherein said polypeptide is at least 80% identical to said amino acid sequence.

Claim 56 (New): The fusion construct of Claim 9, wherein said polypeptide is at least 90% identical to said amino acid sequence.

Claim 57 (New): The fusion construct of Claim 9, wherein said polypeptide is at least 95% identical to said amino acid sequence.